Chao et al. Critical Care 1997, 1:101
http://ccforum.com/

CRITICAL CARE

RESEARCH Open Access

Impact of renal dysfunction on weaning from prolonged mechanical ventilation

David C Chao, David J Scheinhorn, Meg Stearn-Hassenpflug

Abstract

Background: In the intensive care unit (ICU) setting, the combination of mechanical ventilation and renal replacement therapy (RRT) has been associated with prolonged length of hospital stay, high cost of care and poor outcome. We gathered outcome data on patients who had severe renal dysfunction on transfer to our regional weaning center (RWC) for attempted weaning from prolonged mechanical ventilation (PMV). We screened the admission laboratory values of 1077 patients transferred to our RWC over an 8-year period. We reviewed the medical records of patients with serum creatinine > 2.5 mg/dl.

Results: Sixty-three patients met screening criteria and 40 patients were on RRT at the time of transfer. Eighteen patients had begun chronic RRT at least 2 months prior to admission to the transferring hospital for their current illness. Twenty-two patients had RRT initiated at the transferring hospital. Ten patients had RRT initiated at the RWC; eight patients had improvement or resolution of azotemia at our facility. RRT was withheld at patient/family request in five patients with progressive renal failure. None of the 50 patients who received RRT recovered renal function during treatment at our RWC. Intermittent hemodialysis was the standard RRT at the RWC. Duration of mechanical ventilation prior to transfer to the RWC was 49.7 ± 33.5 days (mean ± SD).
Outcome of weaning attempts in the 63 patients was as follows: 13% weaned, 3% failed to wean and 84% died. These outcomes were significantly worse ($P<0.001$) than those in the 1014 patients whose admission serum creatinine was = 2.5 mg/dl (58% weaned, 15% failed to wean, 27% died). The five patients in whom RRT was withheld were predominantly in progressive multisystem organ failure, and were unlikely to have survived regardless of RRT. From the study cohort, only one of the 10 patients discharged alive returned home, in contrast to 42% of the control group. No patient with severe renal dysfunction survived to 1 year post-discharge, compared to a 1-year survival of 38% in the control group ($P = 0.029$). Only four of the 10 patients survived more than 1 month, with the longest survival being 122 days.

Conclusions: Patients who require PMV and RRT have a very poor prognosis. The small number of patients with renal insufficiency not requiring RRT had a more favorable hospital outcome and mortality, but long-term survival remained poor.

hemodialysis patient outcome, prolonged mechanical ventilation, renal failure, renal replacement therapy, respiratory failure, ventilator weaning

Introduction

In the critical care unit, there is a strong correlation between the number of failing organ systems and mortality [1-3]. Patients with both renal and respiratory failure, requiring concurrent mechanical ventilation and renal replacement therapy (RRT), have prolonged length of hospital stay, high cost of care, and a poor outcome [4-6]. This relationship has not been studied in the post-intensive care unit (ICU) setting.

Barlow Respiratory Hospital (BRH) functions as a regional weaning center (RWC), accepting and attempting to wean patients from prolonged mechanical ventilation (PMV). Patients are transferred to BRH from the ICU's of surrounding hospitals after 4-6 weeks of ventilator dependency. These patients typically have chronic respiratory impairment exacerbated by a serious acute

Barlow Respiratory Hospital, Barlow Respiratory Research Center, 2000 Stadium Way, Los Angeles, CA 90026-2696, USA

illness, such as infection, cardiac event, or surgical catastrophe.

We previously reported a significant difference between the admission blood urea nitrogen (BUN) and serum creatinine of patients who weaned and those who remained ventilator-dependent or died [7]. In this study, we gathered outcome data on the cohort of ventilator-dependent patients with severe renal dysfunction on admission to our RWC in order to further elucidate the impact of renal dysfunction on weaning from PMV.

Methods

We retrospectively reviewed the medical records of 1077 patients transferred to our RWC from 1988 to 1996. All patients with admission serum creatinine > 2.5 mg/dl were included in the severe renal dysfunction cohort. Patients with admission serum creatinine = 2.5 mg/dl served as controls. We recorded demographic data, admission blood chemistries and blood gas results. The onset and etiologies of respiratory and renal failures were assessed and recorded based on the transfer records. We reviewed the patients' hospital course at the RWC and scored outcomes of weaning efforts (weaned, failed to wean, died) upon discharge. We tabulated disposition and survival data obtained from post-discharge follow-up records.

All dialysis patients were followed by board-certified nephrologists who wrote the dialysis orders exclusively. Maintenance RRT utilized conventional intermittent hemodialysis for 2-4 h three times a week, consistent with routine practice in the United States. Bicarbonate-based dialysate and cellulose membranes were predominantly used.

Demographic data and selected laboratory values from the two cohorts were compared and reported in terms of mean ± SD for normally distributed data, and median (range) for non-normal distributions. Statistical analysis included the following tests: Student's *t*-tests for age, serum albumin, BUN, creatinine, alveolar-arterial pressure difference [$P(A\text{-}a)O_2$], pH; Wilcoxon Rank Sum tests for comparisons of median times spent ventilator-dependent prior to and during a patient's RWC stay and Fisher's Exact test for comparing weaning outcome and disposition results.

Results

Sixty-three patients met the screening criteria. Forty patients were receiving RRT at admission to our RWC. Of the 23 patients meeting the screening criteria, but not on RRT on admission, eight (35%) had improvement or recovery of renal function while 15 experienced persistent decline to the point where RRT was indicated. Although most cases of renal failure were acute or acute on chronic, none of the 50 patients receiving RRT experienced recovery of renal function. Selected measurements on RWC admission for the study and control groups are shown in Table 1.

Table 2 lists the etiologies of both acute and chronic causes of renal dysfunction identified from the patients' transfer records. Incomplete records and the patients' lengthy hospital courses made identification of a single specific cause of renal dysfunction difficult. Furthermore, acute insult(s) were often superimposed on underlying renal insufficiency. Typically, renal function declined during the course of sepsis or presumed sepsis, borderline or frank hypotension, the peri-operative or post-resuscitation period, and while receiving multiple medications with potential renal toxicity.

Outcomes of weaning attempts in patients with renal dysfunction (13% weaned, 3% failed to wean, 84% died) contrasted with the 1014 control patients (58% weaned, 15% failed to wean, 27% died; $P < 0.001$). Specific weaning outcomes for subgroups of patients are listed in Table 3. Overall outcome comparison is shown in Table

Table 1 Comparison of demographics and selected measurements in PMV patients with and without renal dysfunction

	With renal dysfunction (study group; $n = 63$)	without renal dysfunction (control group; $n = 1014$)	P
Days of mechanical ventilation prior to transfer	42 (6-170)	33 (0-395)	0.04
Gender (% female) 53.1%	56.6%	0.61	
Age	69.7 ± 11.3	69.1 ± 12.8	0.96
Serum albumin (g/dl)	2.72 ± 0.53	2.61 ± 0.60	0.06
Creatinine (mg/dl)	4.36 ± 1.69	0.86 ± 0.45	< 0.001
BUN (mg/dl)	78.6 ± 29.1	26.6 ± 18.2	< 0.001
COPD as primary reason for PMV	12.7%	24.5%	0.015
$PaCO_2$	39.4 ± 9.4	46.9 ± 12.2	< 0.001
$P(A\text{-}a)O_2$ (mmHg)	107.7 ± 58.0	120.4 ± 74.2	0.26
pH	7.41 ± 0.07	7.43 ± 0.07	0.09

BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; PMV = prolonged mechanical ventilation; $PaCO_2$ = partial pressure of arterial carbon dioxide; $P(A\text{-}a)O_2$ = alveolar-arterial pressure difference.

Table 2 Determinants of dysfunction in PMV patients: underlying factors and acute insults

Underlying renal insufficiency	Acute insults
Age	Post-surgical (mostly post-CABG)
Diabetes	Cardiac arrest
Hypertension	Sepsis/MOSF
Congestive heart failure	Hypotension
Renal artery stenosis	Antibiotic toxicity
Renal allograft dysfunction	Renal allograft rejection
Glomerulonephritis	Cholesterol emboli

MOSF = multiple organ system failure; PMV=prolonged mechanical ventilation; CABG=coronary artery bypass graft.

Table 4 Comparison of outcome and 1 year survival in PMV patients with and without renal dysfunction

	Renal dysfunction group (n = 63)	Control group (n = 1014)	P
Weaning outcome:			
Weaned	13%	58%	
Failed to wean	3%	15%	< 0.001
Died	84%	27%	
Time to wean at BRH (days)	36 (22-177)	29 (1-226)	0.13
Alive 1 year post discharge	0%	37.2%	0.029

PMV = prolonged mechanical ventilation; BRH = Barlow Respiratory Hospital.

4. Only patients who stabilized or recovered renal function had outcomes comparable to the control group (4 out of 8; 50%). There was no significant difference in time taken to wean between the two groups: 36 days (22-177) for those with renal dysfunction compared to 29 days (1-226) for the control patients (P = 0.13). Ten of the 63 patients wee discharged alive, but only one was able to return home, with the remainder being discharged to extended care facilities. Post-discharge follow-up of the 10 patients showed that only four survived more than 1 month. No patient with renal dysfunction achieved 1-year survival, with 122 days being the longest post-discharge survival in that cohort. In the control group, 42% were discharged home and 37.2% of all discharges were alive at 1 year.

Discussion

There has been increasing emphasis, partly due to a changing medical economic environment, on research into ICU outcomes and outcome prediction. Aside from the potential to influence resource utilization policy, such data have immediate benefit to clinicians, patients and families, enabling them to make more informed decisions. While outcome studies of mechanically ventilated ICU patients have proliferated, data on PMV patients in the post-ICU setting have been sparse. Patients with PMV consume a disproportionate amount of ICU resources [8,9]. One cost-saving strategy is to transfer these patients, often chronically critically ill, to a long-term acute-care facility such as an RWC. We have described the PMV patient population and outcome at our RWC in two previous articles [10,11]. The concurrent development of renal failure with the requirement for RRT further complicates and increases the cost of care [5].

Sixty-three of 1077 ventilator-dependent patients had concurrent severe renal dysfunction on admission to our RWC; 40 of them were receiving RRT. We found that patients with renal dysfunction spent significantly more time in the ICU than controls prior to transfer to our RWC. They are also less likely to have chronic obstructive pulmonary disease as the primary reason for PMV. The extended ICU stays are most likely a reflection of higher acuity resulting in increased interventions. We found that the majority of these patients were not RRT-dependent prior to ICU entry, but had incurred various renal insults during the course of treatment, not unlike the lung injuries leading to PMV. The etiology of renal dysfunction was often multifactorial with acute insult(s) usually superimposed on chronic renal insufficiency. Although most patients developed acute renal failure necessitating RRT, none had recovery of renal function.

We found that the combination of PMV and severe renal dysfunction on transfer to our RWC forecast a very poor outcome. This mirrors the findings in the ICU setting by Tafreshi *et al* [6], who scored outcomes for 52 ICU patients with 2 weeks of simultaneous mechanical ventilation and RRT. In that study, only three patients (6%) survived to discharge, and none were weaned. Another study by Kraman *et al* found that 74

Table 3 Outcomes of weaning attempts in patients with renal dysfunction, by sub-group

Sub-group	n	Weaned	Failed to wean	Died
RRT initiated > 2 months prior to initial hospitalization	18	1	1	16
RRT initiated at transferring facility and continued at RWC	22	3	1	18
RRT initiated at RWC	10	0	0	10
RRT indicated but withheld	5	0	0	5
RRT not indicated	8	4	0	4
Total	63	8	2	53

RRT = renal replacement theraphy; RWC = regional weaning center.

of 686 respiratory failure patients developed concurrent renal failure in the ICU, with a mortality of 80% [12]. We found an overall weaning success rate of 8% for patients with concurrent mechanical ventilation and RRT. None of the 10 patients who had RRT initiated at BRH weaned or survived to discharge, possibly reflecting progressive and irreversible organ function decline despite treatment.

All five patients in whom RRT was withheld despite the medical indication for dialysis were in progressive multiple organ system failure (MOSF), with the decision not to initiate treatment based on a grave short-term prognosis. It is reasonable to assume that RRT would not have altered the outcome of this group. This assumption is based on the following:

1. mortality in renal failure is strongly dependent on comorbid conditions [1];

2. renal failure contributes to mortality independent of the fluid and metabolic derangements treated with RRT [13,14], and

3. despite treatment of the underlying trigger of MOSF (sepsis in these cases), and aggressive supportive therapy, the renal failure was progressive and irreversible.

Eight of the 23 patients with admission serum creatinine levels >2.5 mg/dl, but not on RRT, experienced stabilization or improvement of renal function. Four of the eight patients (50%) weaned, possibly because better renal function improved their ability to manage fluid balance, reported in our patients to improve weaning success [15]. Despite weaning outcomes similar to that of the controls, their long-term prognosis was uniformly poor, as it was for all groups. Of the 10 patients discharged alive, the longest survival was only 22 days. Although functional status was not specifically studied, the unfavorable disposition (only one of the 10 discharged patients went home) and short survival imply a very low functional capacity and quality of life.

It is possible that improvement in survival can be achieved with newer methods of RRT, such as the use of biocompatible membranes and continuous RRT techniques [16,17]. Relative reduction in risk of death, however, is expected to be low in view of the multiple comorbid conditions in this population. Since these patients have already achieved hemodynamic stability to transfer out of the ICU setting, the indication for continuous RRT is less apparent.

We think our results have broader clinical relevance than for the RWC alone. On the day of transfer to the RWC, the ICU team has decided the next level of care in the critical care continuum, and whether weaning efforts should continue. Caution should be exercised, however, in applying our findings to patients early in the ICU stay, in whom renal dysfunction commonly develops, but may resolve before discharge. Also, we did not capture the cohort of patients who had normal renal function on RWC admission but developed renal failure during our treatment; their prognosis remains to be studied.

Conclusion

Patients with PMV and concurrent severe renal dysfunction on transfer to the RWC have an extremely poor prognosis for weaning outcome and both short- and long-term survival. The duration of mechanical ventilation in the ICU prior to transfer to the RWC was significantly longer where renal dysfunction also developed. Time to wean tended to be longer in the few patients with renal dysfunction who did wean. The small number of PMV patients with renal insufficiency not requiring RRT had a better weaning success rate and mortality than those receiving RRT, but long-term survival was still poor.

Received: 27 June 1997 Revised: 27 October 1997
Accepted: 27 November 1997 Published: 22 January 1998

References

1. Eiseman B, Beart Norton L: **Multiple organ failure.** *Surg Gynecol Obstet* 1977, **144**:323-326.
2. Knaus WA, Draper EA, Wagner DP, *et al*: **Prognosis in acute organ system failure.** *Ann Surg* 1985, **202**:685-693.
3. Rauss A, Knaus WA, Patois E, *et al*: **Prognosis for recovery from multiple organ system failure: the accuracy of objective estimates of chances for survival.** *Med Decis Making* 1990, **10**:155-162.
4. Chertow GM, Christiansen CL, Cleary PD, *et al*: **Prognostic stratification in critically ill patients with acute renal failure requiring dialysis.** *Arch Intern Med* 1995, **155**:1505-1011.
5. Gilbertson AA, Smith JM, Mostafa SM: **The cost of an intensive care unit: a prospective study.** *Intensive Care Med* 1991, **17**:204-208.
6. Tafreshi M, Schneider RF, Rosen MJ: **Outcome of patients who require long-term mechanical ventilation and hemodialysis.** *Chest* 1995, **108**:134S.
7. Scheinhorn DJ, Hassenpflug M, Artinian BM, LaBree L, Catlin JL: **Predictors of weaning after 6 weeks of mechanical ventilation. .** *Chest* 1995, **107**:500-505.
8. Cohen IL, Booth FVM: **Cost containment and mechanical ventilation in the United States.** *New Horizons* 1994, **2**:283-290.
9. Daly RJ, Rudy EB, Thompson KS, *et al*: **Development of a special care unit for chronically critically ill patients.** *Heart Lung* 1991, **20**:45-52.
10. Scheinhorn DJ, Artinian BA, Catlin J: **Weaning from prolonged mechanical ventilation, the experience at a regional weaning center.** *Chest* 1994, **105**:534-539.
11. Scheinhorn DJ, Chao DC, Stearn-Hassenpflug M, LaBree LD, Heltsley DJ: **Post-ICU mechanical ventilation - treatment of 1123 patients at a regional weaning center.** *Chest* 1997, **111**:1654-659.
12. Kraman S, Khan F, Patel S, Seriff N: **Renal failure in the respiratory intensive care unit.** *Crit Care Med* 1979, **7**:263-266.
13. Levy EM, Viscoli CM, Horwitz RI: **The effect of acute renal failure on mortality. A cohort analysis.** *JAMA* 1996, **275**:1489-1494.
14. Turney JH: **Acute renal failure - a dangerous condition.** *JAMA* 1996, **275**:1516-1517.

15. Scheinhorn DJ: **Increase in serum albumin and decrease in body weight correlate with weaning from prolonged mechanical ventilation.** *Am Rev Respir Dis* 1992, **145**:A522.
16. Neveu H, Kleinknecht D, Brivet F, Loirat P, Landais P: **Prognostic factors in acute renal failure due to sepsis. Results of a prospective multicentre study. The French Study Group on Acute Renal Failure.** *Nephrol Dial Transplant* 1996, **11**:293-299.
17. Simpson HKL, Allison MEM, Telfer ABM: **Improving the prognosis in acute renal and respiratory failure.** *Renal Failure* 1987, **10**:45-54.

doi:10.1186/cc112
Cite this article as: Chao *et al*.: Impact of renal dysfunction on weaning from prolonged mechanical ventilation. *Critical Care* 1997 **1**:101.